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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,780	03/07/2002	Mohamend El-Sherbeini	20519P	9669

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/070,780	El-sherbeini et al
Examiner	**Art Unit**
Portner	1645

-- *Th MAILING DATE of this communication appears on th c ver sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Mar 7, 2002* .

2a)☐ This action is **FINAL.** 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 15-17* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 15-17* is/are rejected.

7)☒ Claim(s) *10 and 16* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-11, 15-17 are pending.

Claims 12-14 have been canceled.

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

2. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 120 is acknowledged.

Allowable Subject Matter

3. Claims 10 and 16 define over the prior art of record, and would be allowable upon amendment of the claims to obviate rejections under 35 U.S.C. 112, first and second paragraphs .

Drawings

4. Figure 2 is discussed but did not accompany Figure 1, upon filing the instant Application (see page 85, line 34). The subject matter of this application admits of illustration by a drawing to facilitate understanding of the invention. Applicant is required to furnish a drawing under 37 CFR 1.81. No new matter may be introduced in the required drawing.

Specification

5. The disclosure is objected to because of the following informalities: The specification at pages 20-21 evidences blank lines; information is missing. No new matter should be submitted. Appropriate correction is required.

6. At page 1, lines 4-11, the phrases "CROSS-REFERENCE TO RELATED APPLICATIONS Not applicable"; 'STATEMENT REGARDING FEDERALLY-SPONSORED R&D Not

applicable"; "REFERENCE TO MICROFICHE APPENDIX Not applicable", after which an amendment to refer to other applications has been inserted. This section of the specification is confusing.

7. At page 1, lines 23-24, the phrase --a single molecule composed of peptidoglycan--; why is this phrase set of by "-- --" notations?

Claim Rejections - 35 U.S.C. § 101

8. 35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 5-6 are directed to products that are not isolated and purified; the claimed invention is directed to non-statutory subject matter. Claims 5 and 6 read on a naturally occurring cell and the polynucleotide contained therein.

Claim Rejections - 35 U.S.C. § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-8, 9, 11, 15, 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID Nos: 1-2 and therefore the written description is not commensurate in scope with the claims

drawn to an isolated polynucleotide that encodes a polypeptide molecule that shares any size amino acid sequence of SEQ ID NO 2, nor has the genus of polypeptides that only share any size amino acid sequence of SEQ ID NO 2. The specification does not provide written descriptive support for the claimed invention directed to polynucleotides, polypeptides and the use of these polynucleotides and polypeptides to screen for inhibitors, wherein the polypeptides need only have "an amino acid sequence of SEQ ID NO 2" , which includes fragments of SEQ ID NO 2. Within the scope of the claimed invention are molecules that have no shared biological function, are structural homologs, or allelic variants of SEQ ID No 1 and 2.

The instant specification suggests at page 4, lines 6-8, the claimed polynucleotide and polypeptide are defined by narrative directed to the polypeptide, the polypeptide being defined as "a naturally occurring mutant or polymorphic form of the protein"; this phrase does not provide written descriptive support for the full scope of the invention that comprises a polypeptide sequence has to an amino acid sequence as set forth in SEQ ID NO 2 .

Additionally the specification at page 6, states "Polynucleotides useful in the present invention include those described herein and those that one of skill in the art will be able to derive therefrom following the teachings of the specification". The derived polynucleotides are suggested, and not described.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1 or 2 which encode a Pseudomonas aeruginosa MurC polypeptide, the skilled artisan cannot envision the detailed structure of the polypeptide or a recombinant polypeptide encoded by a polynucleotide and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

However, no disclosure, beyond the mere mention of naturally occurring analogues (natural allelic variants or homologs) is made in the specification or the suggestion of the construction of mutant nucleic acid sequences. This is insufficient to support the generic claims

as provided by the Interim Written Description Guild lines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated and purified polynucleotide of SEQ ID NO 1 which encodes a polypeptide represented by SEQ ID NO 2, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph.

13. Claims 1-8, 9-11, 15-17 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 recite the phrase "having an amino acid sequence of SEQ ID No 2"; what portion of SEQ ID NO 2 has been selected to be encoded by the claimed polynucleotide that has no defined biological function and is not limited to have the entire amino acid sequence of SEQ ID NO 2?

Claim 8 also recites the phrase "having an amino acid sequence of SEQ ID No 2" and is directed to a polypeptide; the polypeptide does not evidence any required biological function, nor any specific structure except a portion of SEQ ID NO 2. What is the claimed isolated polypeptide?

Claims 4 and 10 recite the phrase "the nucleotide sequence of SEQ ID NO 1"; this phrase lacks antecedent basis in independent claim form which they depend.

Claims 5 and 6 are not further limiting of claim 1 from which they directly or indirectly depend, as the products being claims are not isolated and purified, thus broadening the scope of the claim to include products that occur in nature. Claim 5 recites the non-specific article "A", thus not specifically referring back to the polynucleotide of claim 1. Dependence upon claim 1 is used only to define what the polynucleotide is, rather than defining the polynucleotide to be isolated and purified. The invention is not distinctly claimed.

14. The term "relative activity" in claims 9-11, 15-17 is a relative term which renders the claim indefinite. The term "relative activity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

In light of the nature and structure of the candidate compound not being defined, the relative activity of the polypeptide can not be determined. Relative activity is usually determined relative to a known standard not an unknown candidate compound as defined by the phrase "the relative activity of the polypeptide in the presence of the candidate.

As the candidate compound is free to act and interact with any component of the cells, how the activity of the candidate is determined to be a specific inhibitor for MurC is not distinctly claimed. The host cell has not been defined to be a MurC negative host cell, into which an expression vector encoding a MurC polypeptide has been added. MurC polypeptide activity relative to the candidate has not been so claimed as to define the candidate to be specific for the heterologous MurC polypeptide through the recitation of the phrase "to permit the interaction". Any effect observed need not be MurC specific interaction in a cell that comprises many other polypeptides, the candidate would interact. The invention is not distinctly claimed.

Claim Rejections - 35 U.S.C. § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Eveland et al (1997).

(instant claims 1-6) Eveland et al disclose the claimed invention directed to a purified and isolated polynucleotide that will hybridize to and is complementary to a polynucleotide that encodes a polypeptide of SEQ ID No 2 (see page 6225, col. 1, last paragraph, murC 5' and 3' primer pair). Mutant (non-natural) modified nucleotides were inserted by base change into the coding sequence for murC (see Table 4, top of page 6227, host cell strain ST222) resulting in a modified polypeptide.

(instant claim 8) Additionally Eveland et al disclose a polypeptide having an amino acid sequence of SEQ Id NO 2, specifically a polypeptide that comprises, and is encoded by the consensus sequence of the mur genes (see page 6225, col. 2, Results section, highly conserved sequence GXXGK(T/S) and GxxNxxNxxAAxA; also see page 6224, Figure 1, consensus sequences for regions I-IV, MurC polypeptides that comprises an amino acid sequence that is shared in common with SEQ ID NO 2.

Please Note: The examiner is reading the phrase "expression vector" to include a polynucleotide sequence that is a part of a bacterial cell chromosome, and need not be a heterologous expression vector inserted into a host cell.

17. Claims 15 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Chabin et al (US Pat. 5,891,621) in light of Eveland et al (1997).

(Instant claims 15 and 17) Chabin et al disclose the instantly claimed method of determining whether a candidate compound is an inhibitor of a MurC polypeptide that comprises an amino acid sequence of SEQ Id NO 2, the method comprising the steps of:

providing a sample comprising a MurC polypeptide having an amino acid sequence of SEQ ID NO 2 (see col. 7, Scheme 1, col. 7, lines 50-67 "expression vector", line 55 or col. 7,, lines 64-65 through col. 8, lines 1-54; in light of the disclosure of Eveland et al (see Figure 1), the

sequence that encodes the MurC polypeptide of E.coli,(see Chabin et al, Table 1, col. 2, line 18, murC) inherently comprises an amino acid sequence of SEQ Id NO 2, as the amino acid sequence of E.coli and P.aeruginosa MurC contain a consensus sequence that SEQ ID NO 2;

contacting a sample with the candidate to permit incubation with the candidate and the MurC polypeptide; and

determining whether the candidate is an inhibitor of the MurC polypeptide (see Chabin et al, col. 2, lines 58-62 and all claims; col. 9, lines 38-67; col. 10, lines 16-65; col. 13, Example 3, lines 25-36). Chabin et al anticipate the instantly claimed invention.

18. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by WO98/03533 (Oligos etc. and Oligos Therapeutics, Inc., January 29, 1998).
(instant claims 1-2) Oligos etc. disclose the claimed invention directed to a purified and isolated polynucleotide that will hybridize to and is complementary to a polynucleotide that encodes a polypeptide of SEQ ID No 2 (see page 83, Table 1, murC primer , NBT 51, SEQ ID NO 58). The reference anticipates the instantly claimed invention.

19. Claims 1-8, 9, 11, 15 and 17 are rejected under 35 U.S.C. 102(a or e) as being anticipated by Smithkline Beecham Corporation (EP0889123 A2).
(Instant claims 1-8, 9-11, 15 and 17) Smithkline Beecham Corporation disclose the instantly claimed method of determining whether a candidate compound is an inhibitor of a MurC polypeptide that comprises an amino acid sequence of SEQ Id NO 2, the method comprising the steps of:

providing a cell (instant claims 9-11)or a sample (instant claim 15, 17) comprising a MurC polypeptide having an amino acid sequence of SEQ ID NO 2 (instant claims 1-6, and 8) (see Smithkline Beecham Corporation, page 37, claim 6; the sequence that encodes the MurC polypeptide of S.aureus comprises the MurC consensus sequence, see Table 1, page 4 (b), line 2,

GxHGKTxTT) and therefore comprises an amino acid sequence of SEQ Id NO 2, as the amino acid sequence of S.aureus and P.aeruginosa MurC contain a consensus sequence contained in SEQ ID NO 2);

contacting the cell (see Smithkline Beecham Corporation, page 15, lines 40-58, page 16, lines 1-58 through to page 17, lines 1-35; page 11, lines 10-25) or sample (purified polypeptides, see Smithkline Beecham Corporation, page 11, lines 30-35) with the candidate to permit incubation with the candidate and the MurC polypeptide (identification of an antagonist/inhibitor; and

determining whether the candidate is an inhibitor of the MurC polypeptide (see page 17, lines 36-45; see page 16, lines 21-35).Smithkline Beecham Corporation anticipate the instantly claimed invention) relative to a standard (see Smithkline Beecham Corporation, page 16, line 11). Smithkline Beecham Corporation anticipates the instantly claimed invention.

Conclusion

20. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

21. Abdel Aziz El Zoeiby, Ahmed (1999, French abstract) is cited to show Pseudomonas aeruginosa MurC polypeptide, and polynucleotides.

22. Rothstein (US Pat. 6,534,278); Grubler et al (1996); Falk et al (1996); Ikeda, M et al (1990); Jin, H et al(1996); and Liger, D et al (1995) are cited to show uridine diphosphate N-acetyl-muramate:L-alanine ligase (MurC) proteins known in the art.

23. Black et al (Smithkline Beecham Corporation, US Pat. 6,310,193) is cited to show S.pneumoniae MurC polypeptide.

24. JP11-225773 is cited to show an assay for screening for inhibitors of murC (see English translation, assay, all claims.

25.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp

July 13, 2003

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